

intradermal, intramuscular, intraocular, intrathecal, intracerebral, intranasal, infusion, oral, rectal, patch and implant rates.

38. (New) A composition comprising;

(a) an antagonist of the pro-survival Bcl-2 protein family said antagonist generated by the method of a scaffold BH3-only protein structure with residue positions defining an amphipathic α -helix formed by the BH3 domain;

(b) selecting one or more residue positions associated with a promiscuous binding phenotype of a BH3- only protein;

(c) substituting amino acid residues conferring a promiscuous phenotype for amino acids or their chemical analogs which confer a restrictive binding pattern to a Bcl-2 protein; and

(d) analyzing the interaction of each substitution for an ability to induce a more restrictive spectrum of binding to a Bcl-2 protein, said composition further comprising one or more pharmaceutically acceptable carriers and/or diluents.